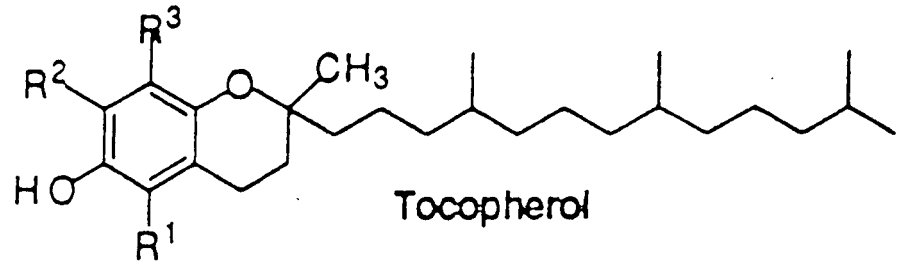
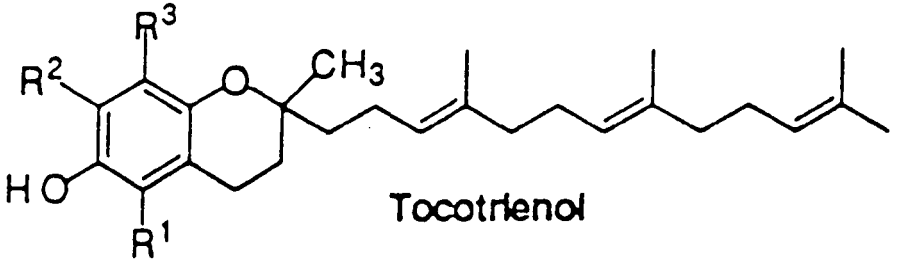


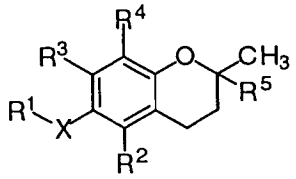
Tocopherol



Tocotrienol

Compound	R^1	R^2	R^3
Alpha (α)	CH_3	CH_3	CH_3
Beta (β)	CH_3	H	CH_3
Gamma (γ)	H	CH_3	CH_3
Delta (δ)	H	H	CH_3

Fig. 1



Compound	R^1	R^2	R^3	R^4	R^5
1	CH_2CO_2H	CH_3	CH_3	CH_3	phytyl
2	$(CH_2)_2CO_2H$	CH_3	CH_3	CH_3	phytyl
3	$(CH_2)_3CO_2H$	CH_3	CH_3	CH_3	phytyl
4	$(CH_2)_4CO_2H$	CH_3	CH_3	CH_3	phytyl
5	$(CH_2)_5CO_2H$	CH_3	CH_3	CH_3	phytyl
6	$(CH_2)_7CO_2H$	CH_3	CH_3	CH_3	phytyl
7	CH_2CO_2H	CH_3	H	CH_3	phytyl
8	CH_2CO_2H	CH_3	H	CH_3	phytyl
9	CH_2CO_2H	H	H	CH_3	phytyl
10	CH_2CONH_2	CH_3	CH_3	CH_3	phytyl
11	$CH_2CO_2CH_3$	CH_3	CH_3	CH_3	phytyl
12	$CH_2CON(CH_2CO2H)_2$	CH_3	CH_3	CH_3	phytyl
13	CH_2CH_2OH	CH_3	CH_3	CH_3	phytyl
14	CH_2CO_2H	CH_3	CH_3	CH_3	CH_3
15	RS CH_2CO_2H	CH_3	CH_3	CH_3	phytyl

Fig. 2A

Compound	R^1	R^2	R^3	R^4	R^5
16	CH_2CO_2H	CH_3	CH_3	CH_3	COOH
17	R/RS CH_2CO_2H	CH_3	CH_3	CH_3	phytyl
18	CH_2CO_2H	CH_3	CH_3	CH_3	isoprenyl
19	NH_3Cl	CH_3	CH_3	CH_3	phytyl
20	CH_2CO_2H	CH_3	CH_3	CH_3	phytyl
21	OSO_3NHEt_3	CH_3	CH_3	CH_3	phytyl
22	CH_2CO_2H	CH_3	CH_3	CH_3	phytyl
23	CH_2CO_2H	CH_3	CH_3	CH_3	phytyl
24	CH_2CO_2H	CH_3	CH_3	CH_3	phytyl
25	CH_2CO_2H	CH_3	CH_3	CH_3	phytyl
26	CH_2CO_2H	CH_3	CH_3	CH_3	other
27	CH_2CO_2H	CH_3	CH_3	CH_3	other
28	CH_2CO_2H	CH_3	CH_3	CH_3	ester
29	CH_2CO_2H	CH_3	CH_3	CH_3	ester

Phytyl =

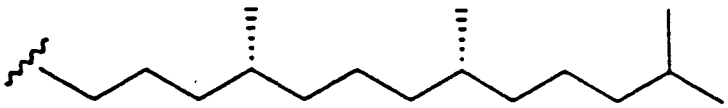
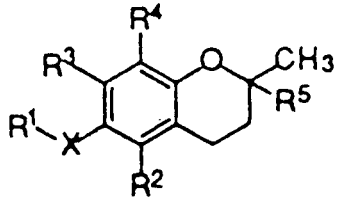
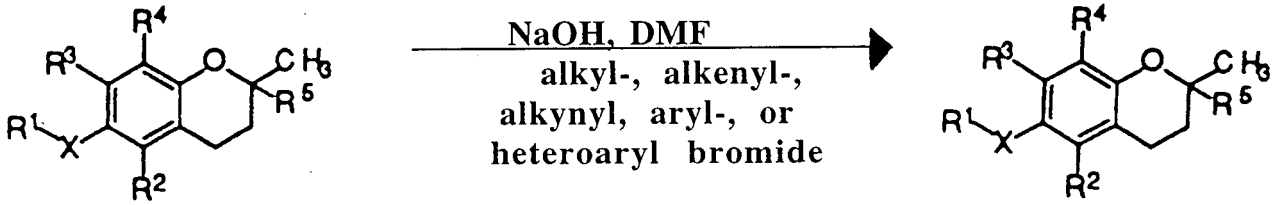


Fig. 2B



where X = O, N, or S
and n = 1 - 10

R^1 = alkyl, alkenyl, akynyl, aryl, and heteroaryl.



R^1 = alkyl, alkenyl, akynyl, aryl, and heteroaryl carboxylic acids or carboxylates.

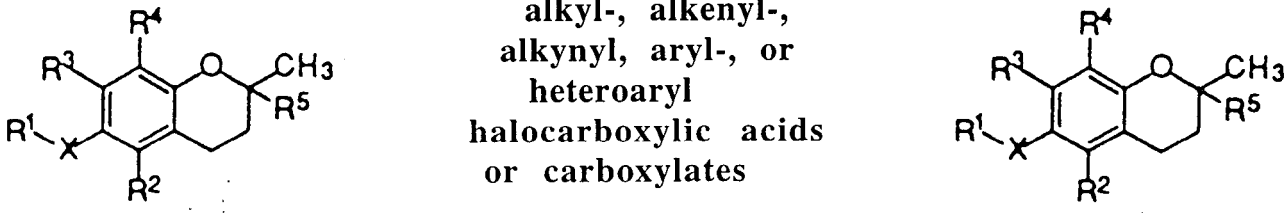
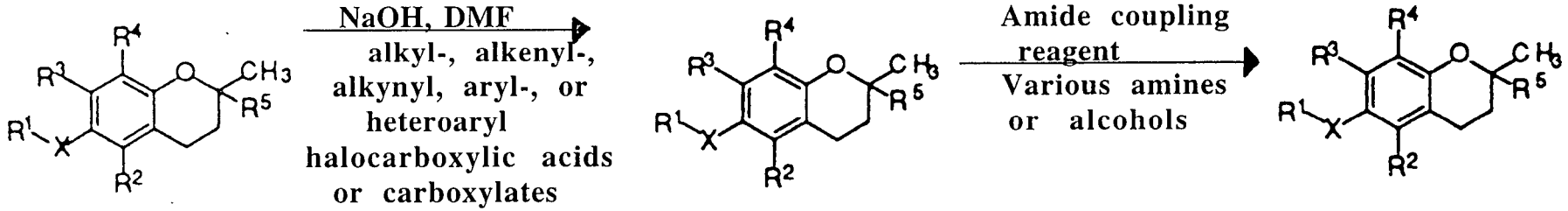


Fig. 3A

R^1 = alkyl, alkenyl, akynyl, aryl, and heteroaryl carboxamides and esters



R^1 = alkyl, alkenyl, akynyl, aryl, and heteroaryl thioamides, thioesters and thioacids.

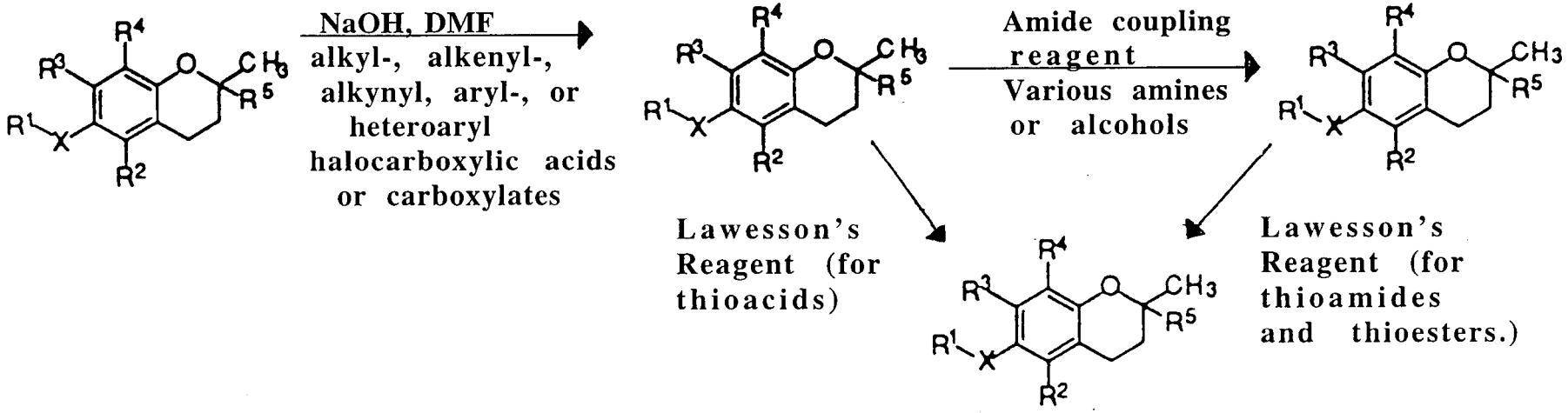
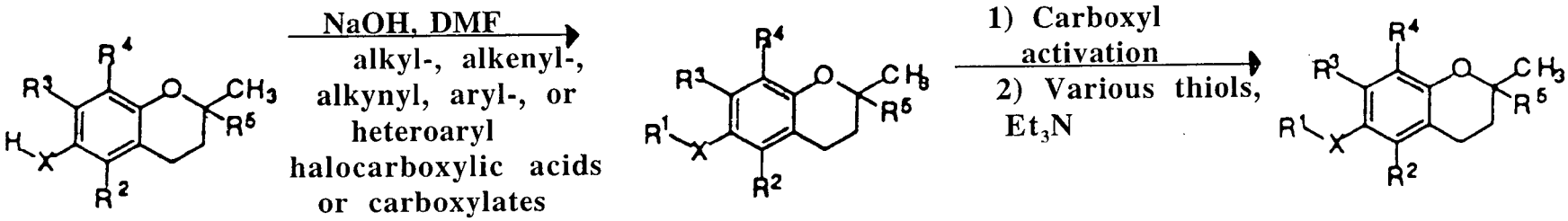


Fig. 3B

R^1 = alkyl, alkenyl, akynyl, aryl, and heteroaryl thiolesters.



R^1 = saccharides or alkyloxy-linked saccharides

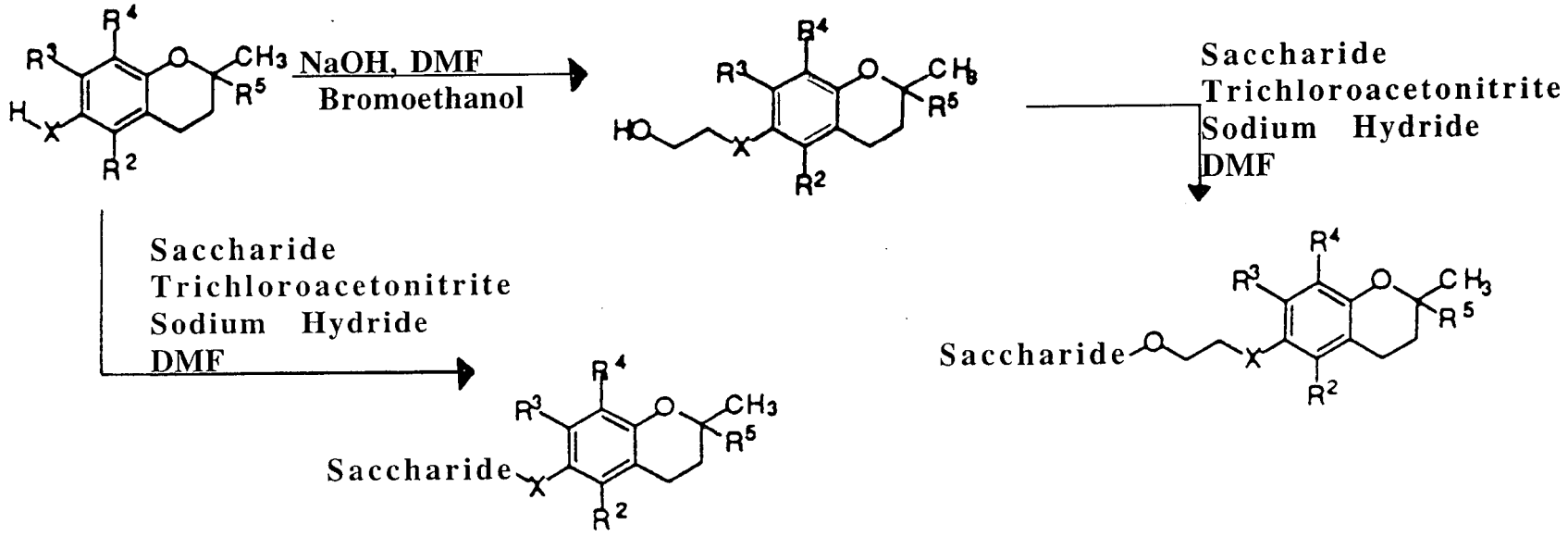
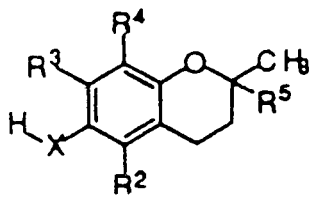


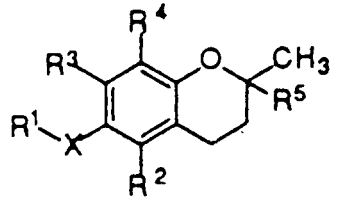
Fig. 3C

R^1 = alkyl, alkenyl, akynyl, aryl, and heteroaryl amines.

alkyl-, alkenyl-, alkynyl, aryl-, or heteroaryl haloamines

1) Di-tert-butyldicarbonate
2) K_2CO_3 DMF



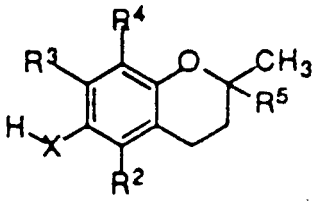


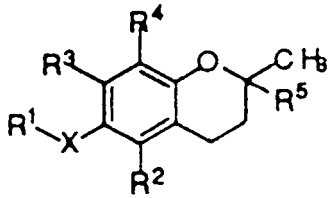
3) Trifluoracetic acid

R^1 = alkyl, alkenyl, akynyl, aryl, and heteroaryl carboxamides.

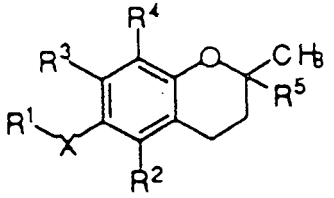
alkyl-, alkenyl-, alkynyl, aryl-, or heteroaryl haloamines

1) Di-tert-butyldicarbonate
2) K_2CO_3 DMF





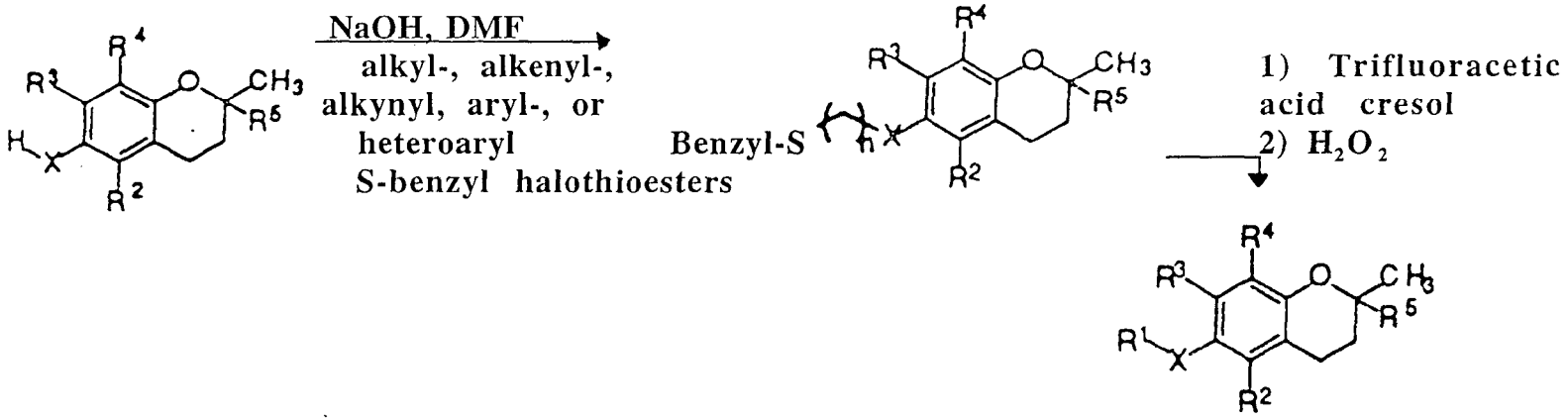
Amide coupling reagent
Various carboxylic acids



3) Trifluoracetic acid

Fig. 3D

R^1 = alkyl, alkenyl, akynyl, aryl, and heteroaryl sulfonates.



R^1 = alkyl, alkenyl, akynyl, aryl, and heteroaryl sulfates.

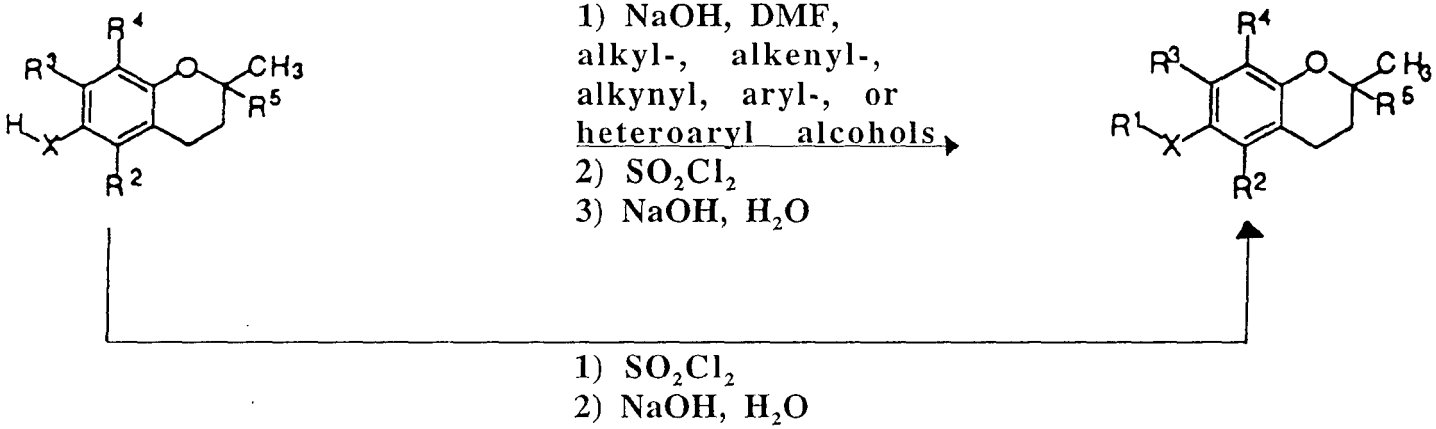
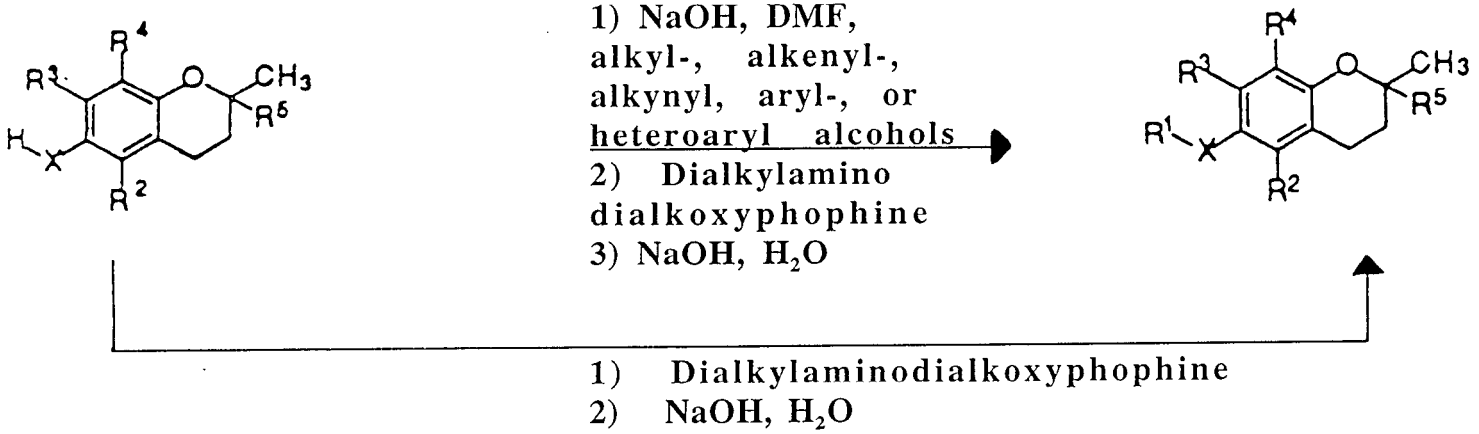


Fig. 3E

R^1 = alkyl, alkenyl, akynyl, aryl, and heteroaryl phosphates.



R^1 = alkyl, alkenyl, alkynyl, aryl, and heteroaryl alcohols, ethers, and nitrites.

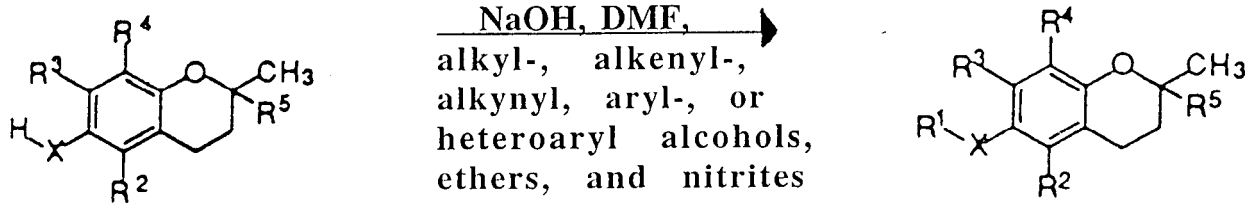
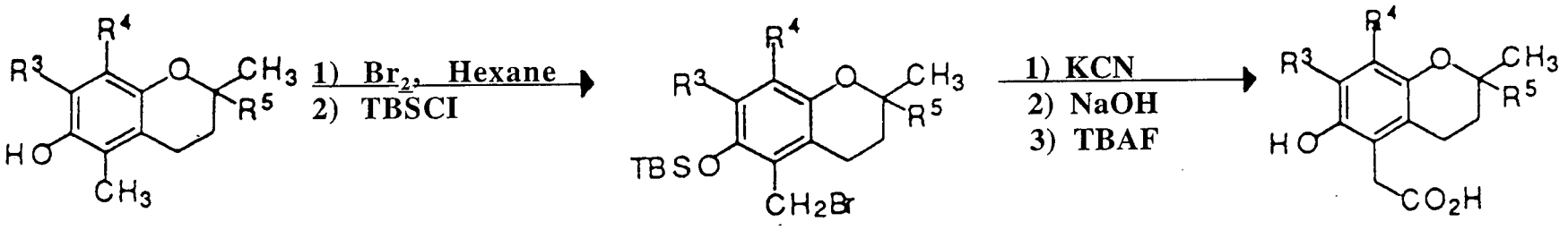


Fig. 3F

R^2 = benzyl carboxylic acid or carboxylate.



R^2 = benzyl carboxamides or esters.

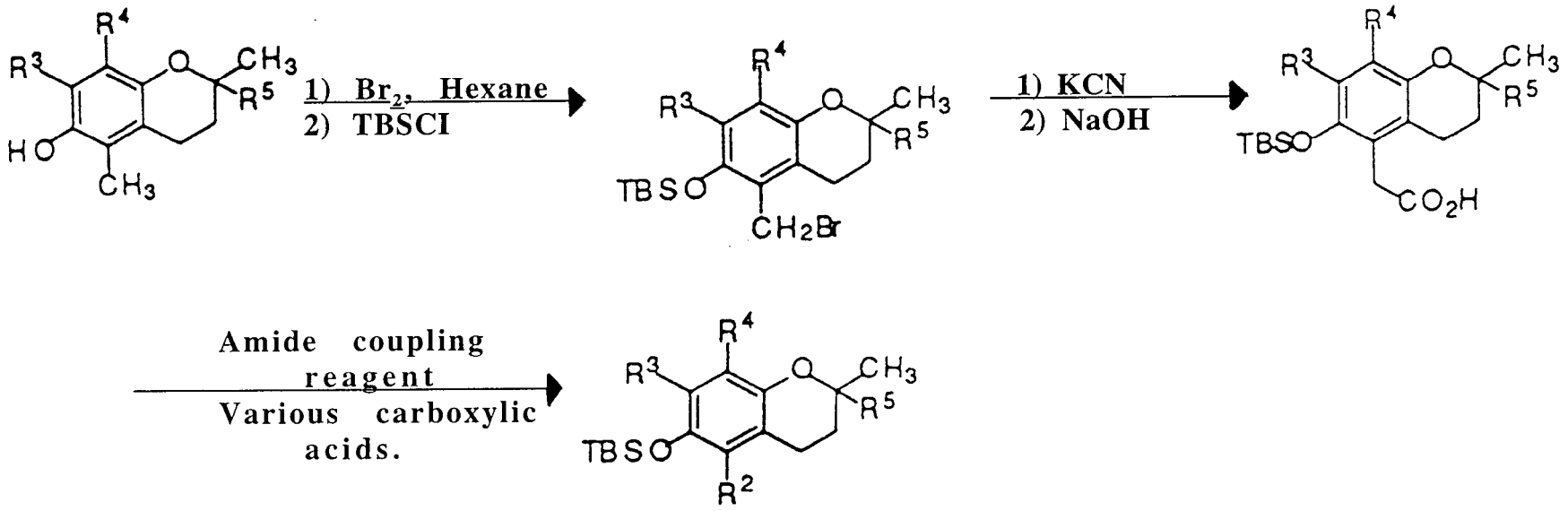
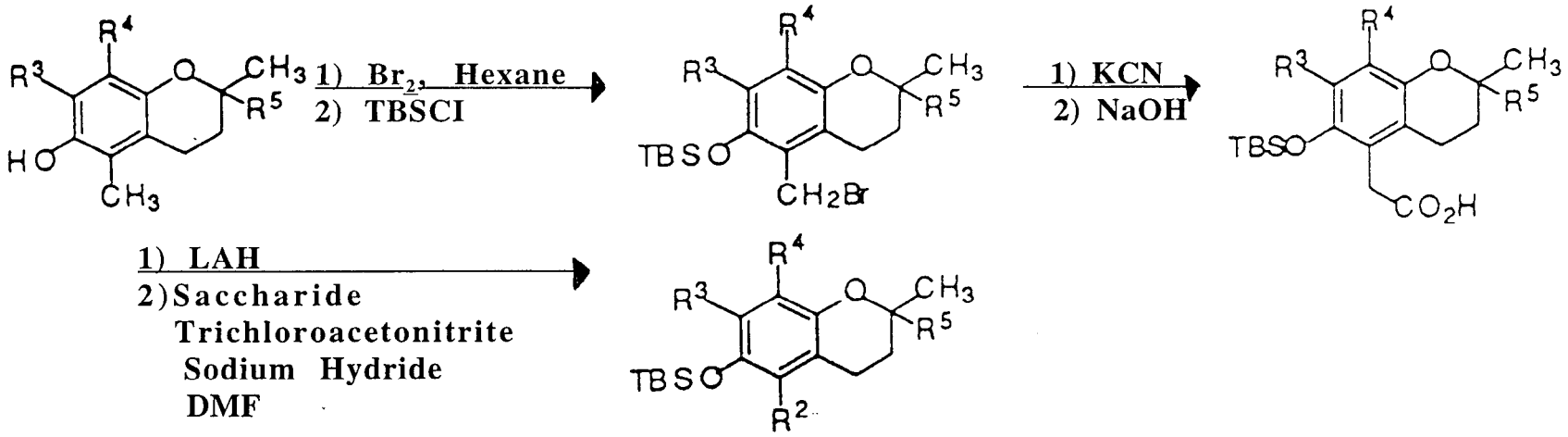


Fig. 4A

R^2 = saccharides.



R^2 = amine

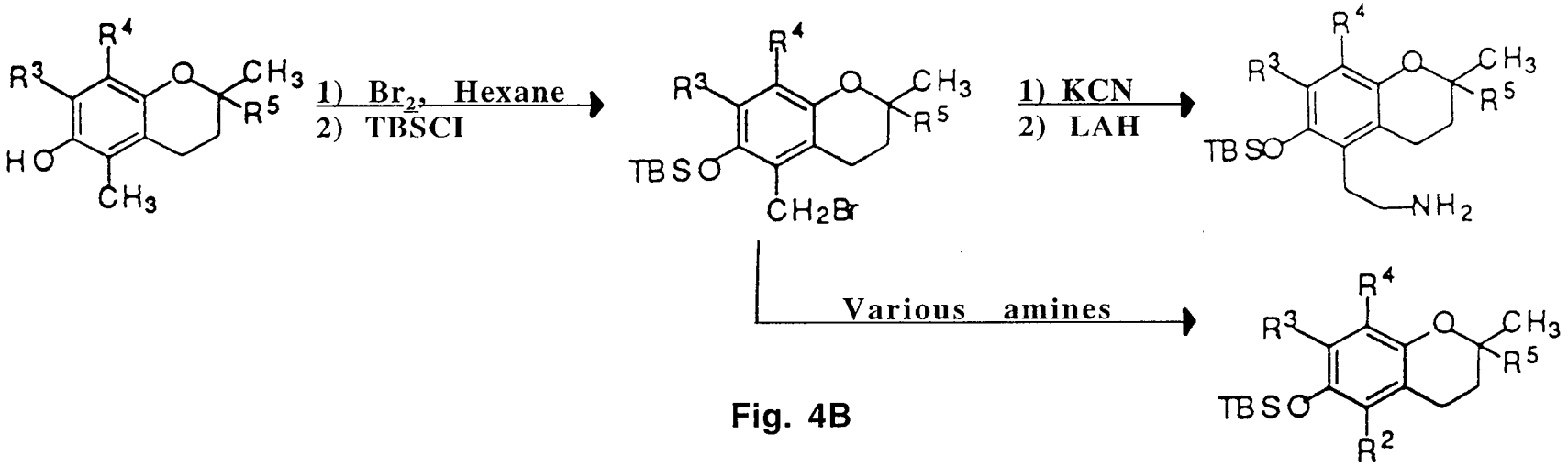
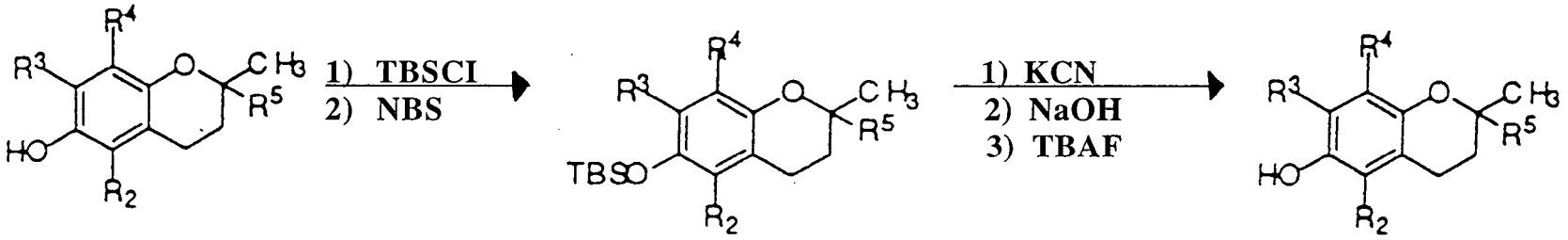


Fig. 4B

R^3, R^4 = benzyl carboxylic acid or carboxylate.



R^3, R^4 = benzyl carboxamides or esters.

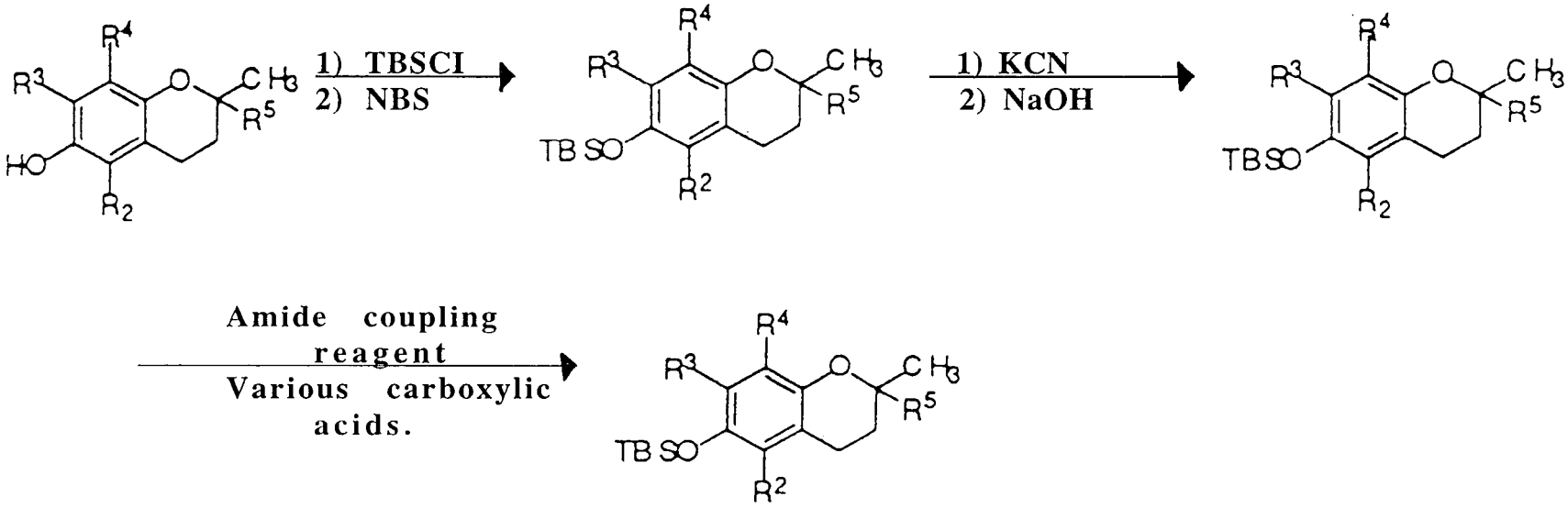
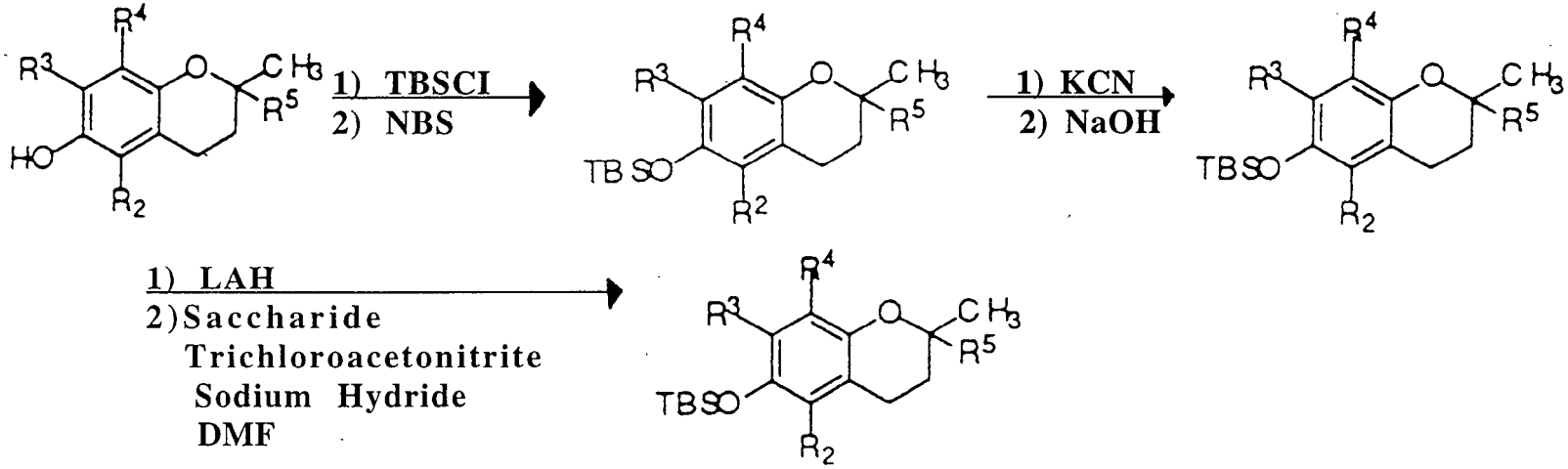


Fig. 5A

R^3, R^4 = saccharides.



R^3, R^4 = amine

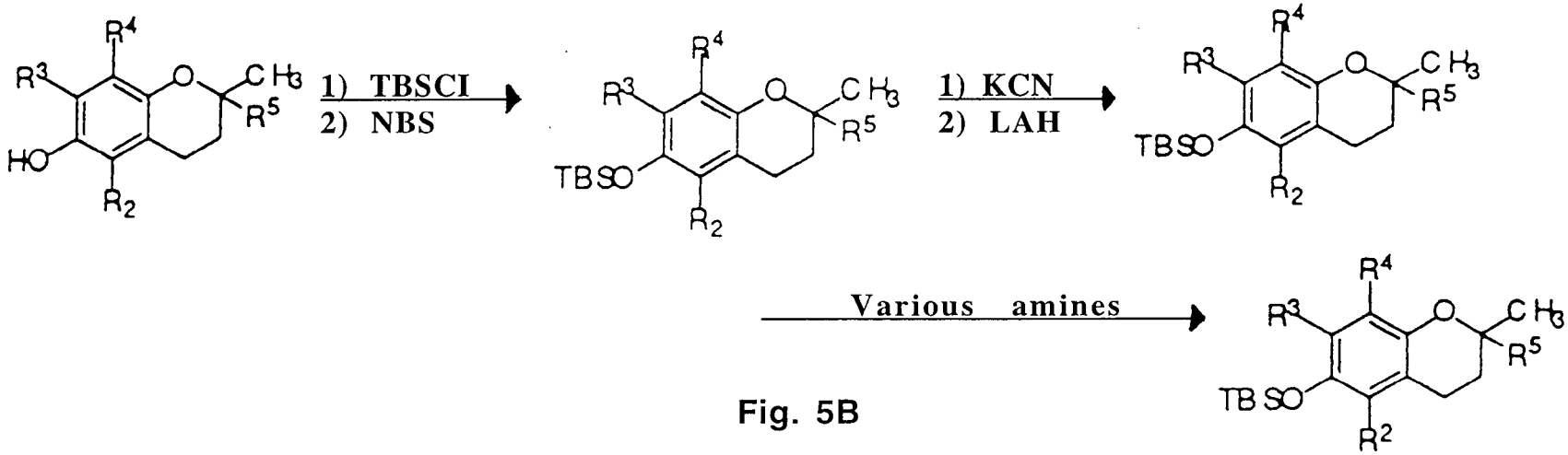
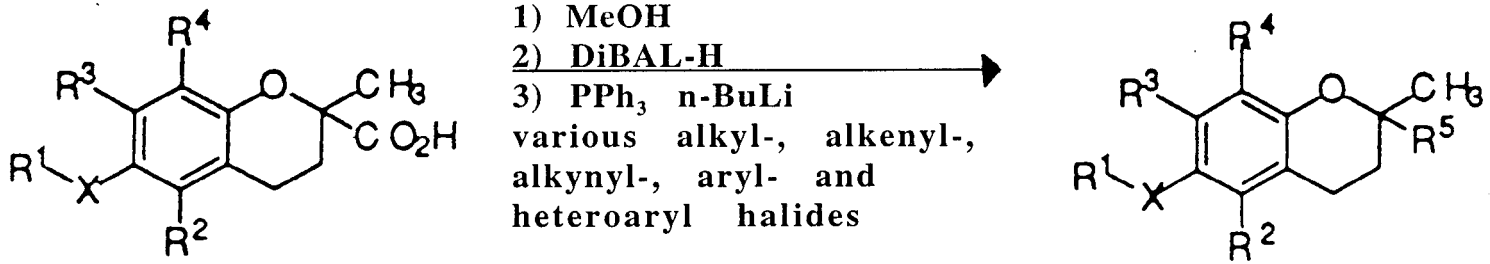


Fig. 5B

R^5 = alkyl, alkenyl, alkynyl, aryl, and heteroaryl.



R^5 = alkyl, alkenyl, alkynyl, aryl, and heteroaryl amides and esters.

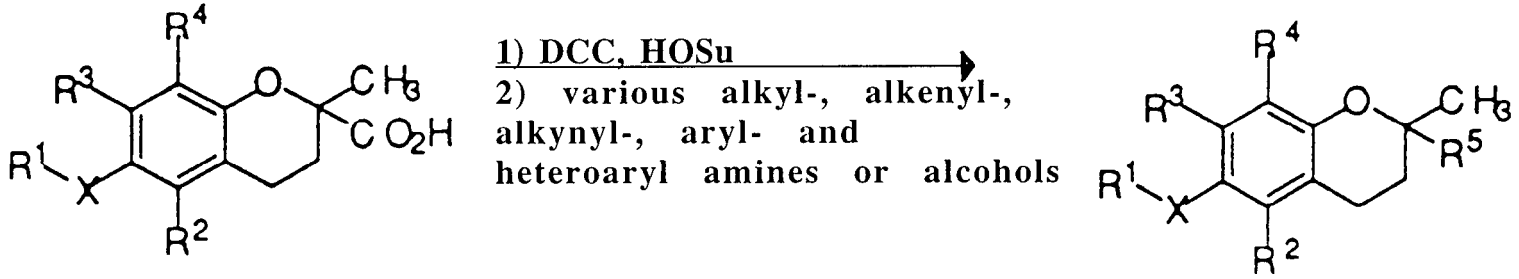
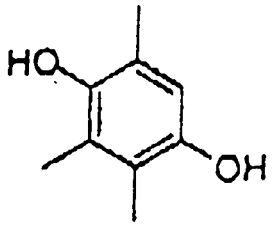


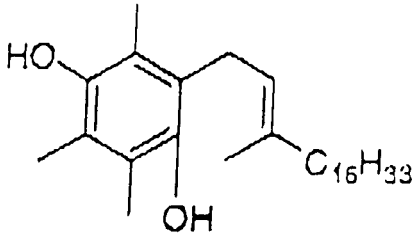
Fig. 6



30

isophytol/anhydrous zinc chloride

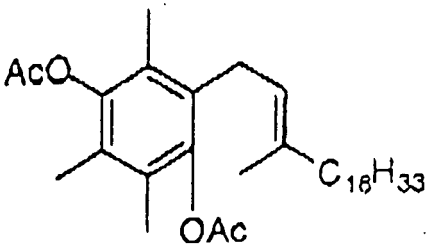
glacial acetic acid in absolute ether
reflux for 1 h



31 (47%)

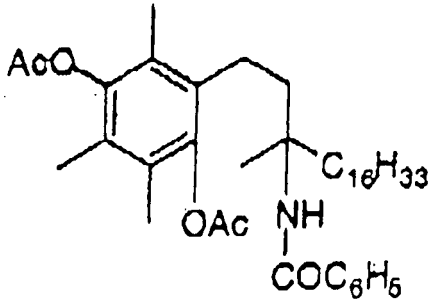
pyridine/acetic anhydride

10 h



32 (95%)

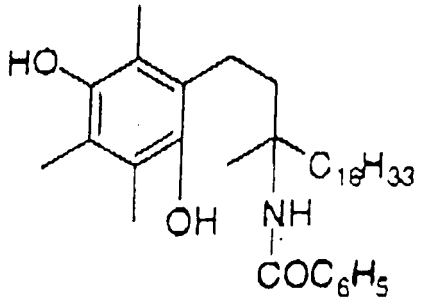
1. C_6H_6CN/H_2SO_4
2. glacial acetic acid/10 h, rt
3. Na_2CO_3



33 (88%)

KOH/MeOH

reflux for 45 min



34 (88%)

Fig. 7A

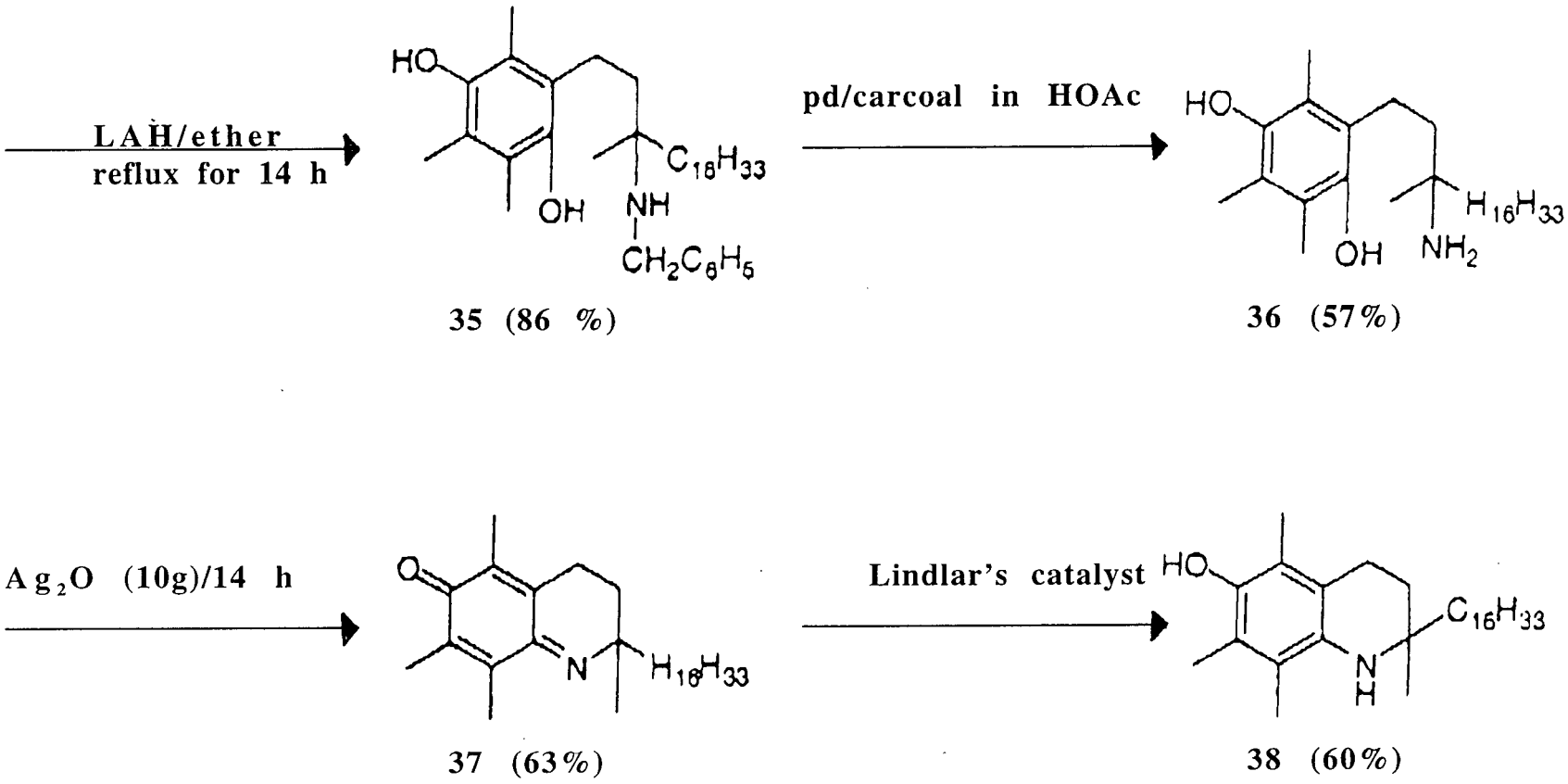


Fig. 7B

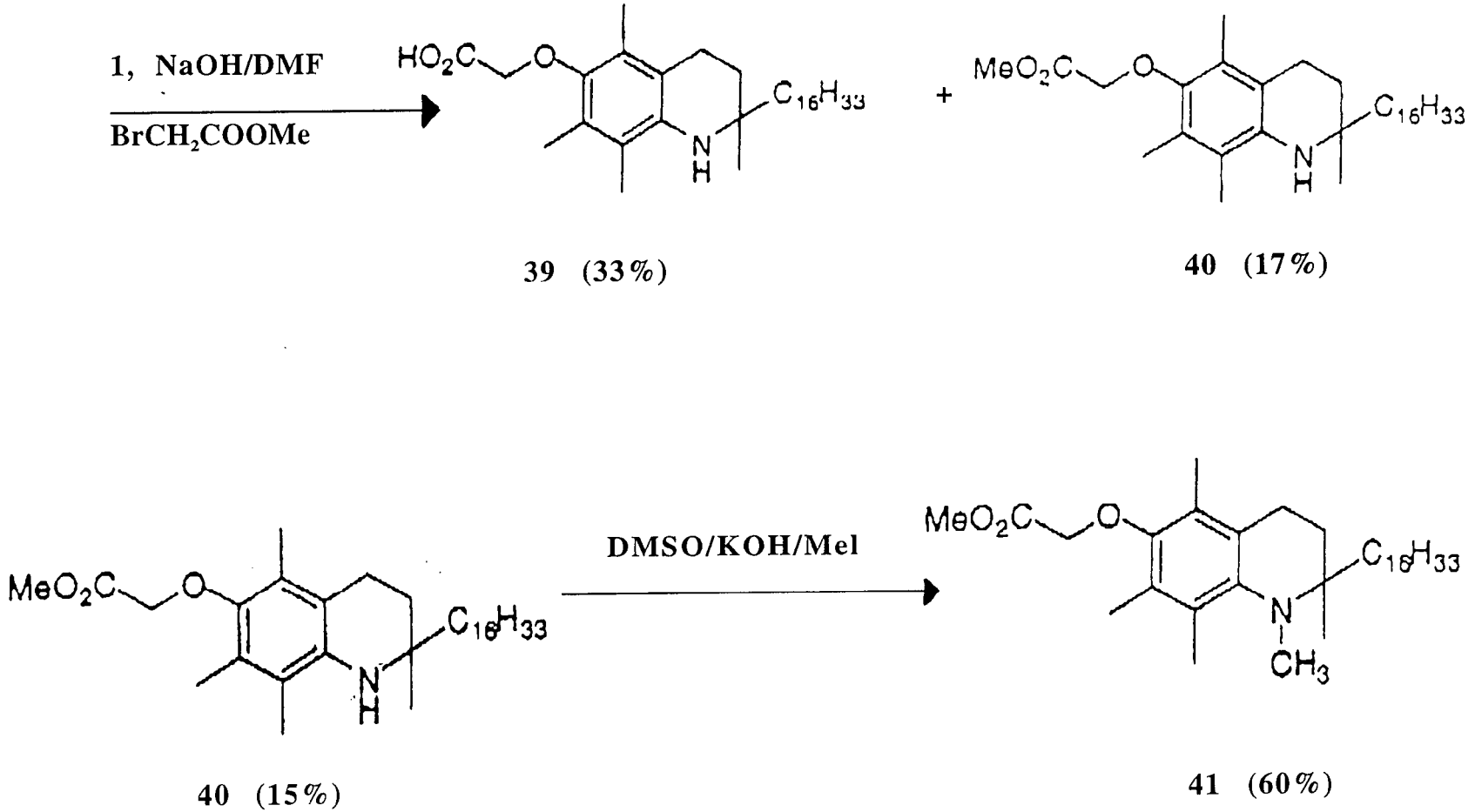
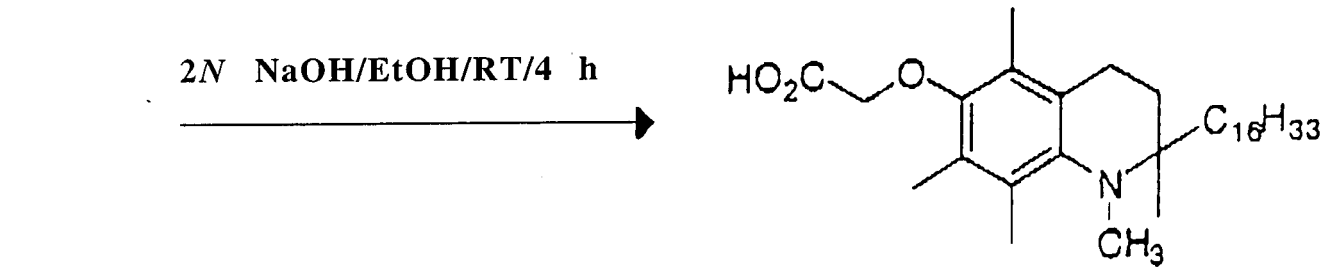
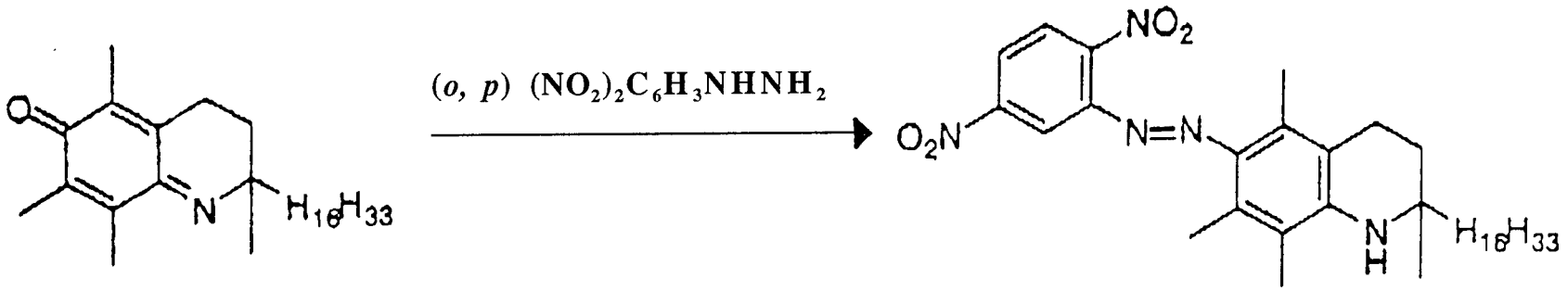


Fig. 7C



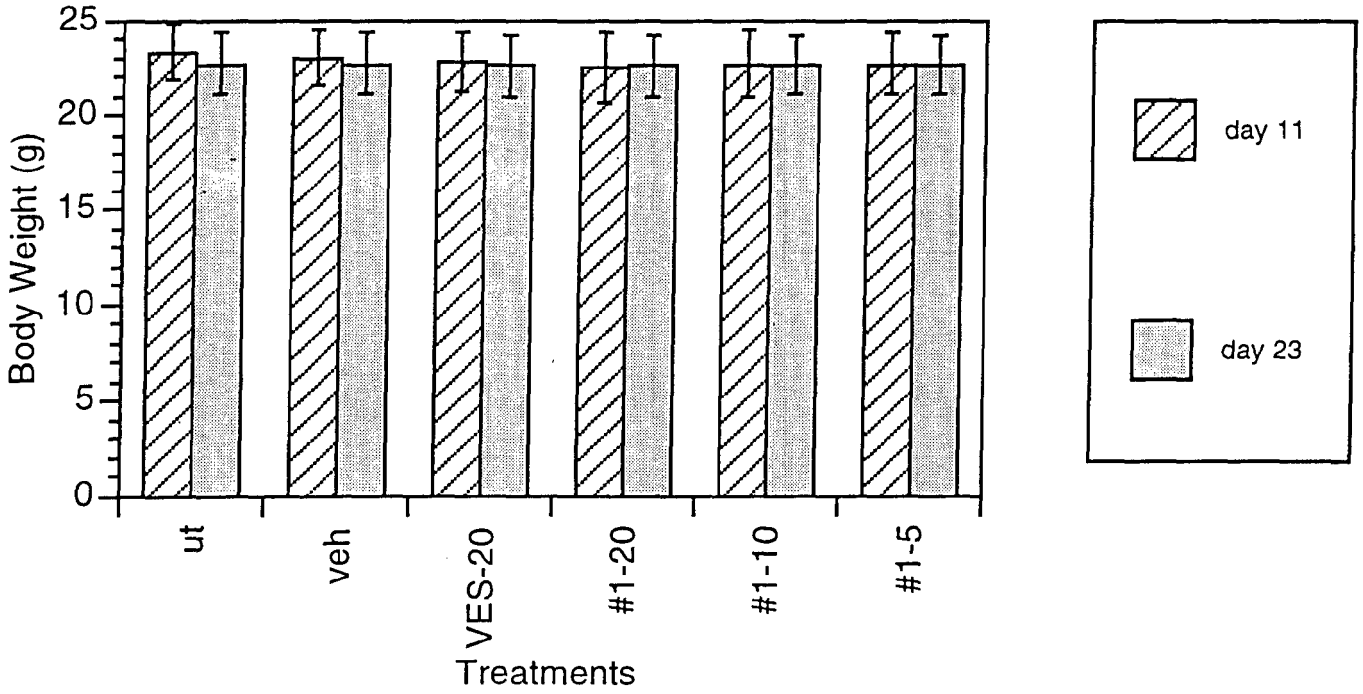
42 (90%)



37 (63%)

43 (95%)

Fig. 7D



Mean body weights of mice +/- S.D. with an n=5
ut = untreated; veh = vehicle control; VES-20 = ester succinated vitamin E at 20 mg/day; #1 = compound #1 at 20, 10, and 5 mg/day.

FIG. 8

MDA MB-435 Human Breast Cancer Cells

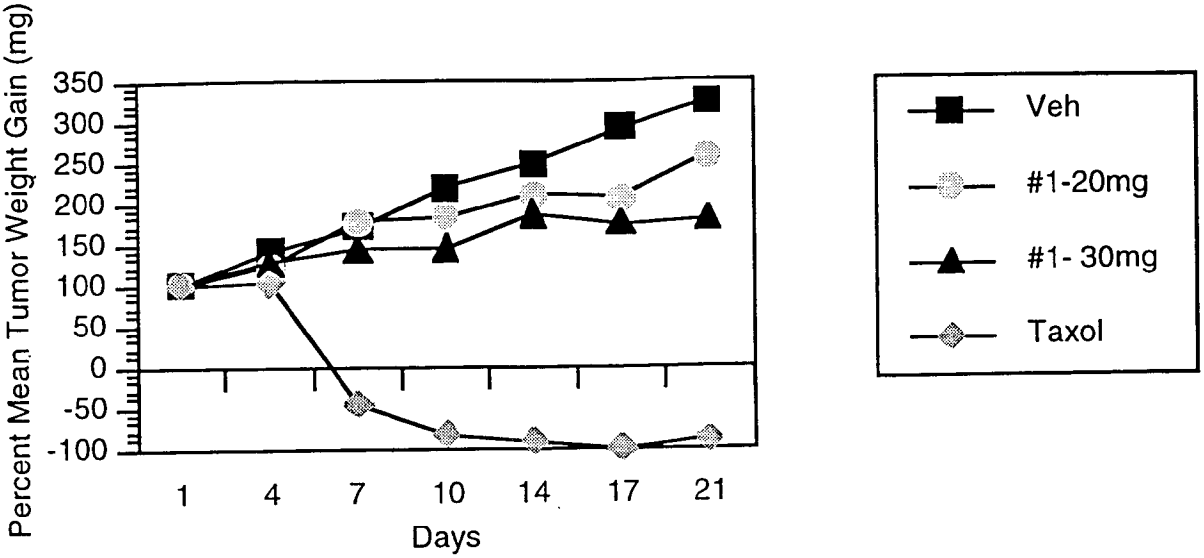


FIG. 9A

DU-145 Human Prostrate Cancer Cells

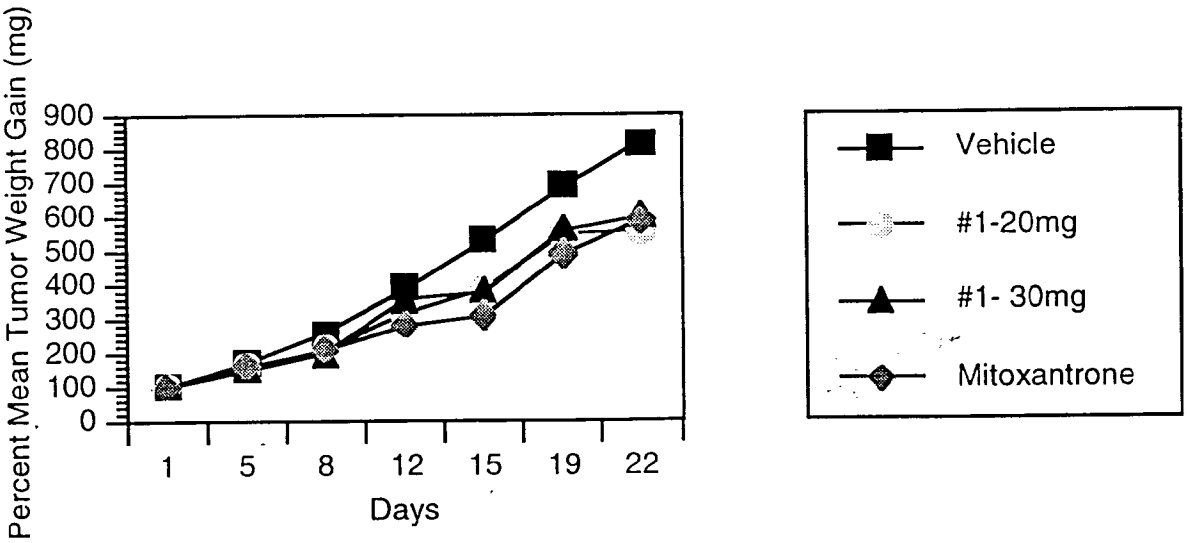


FIG. 9B

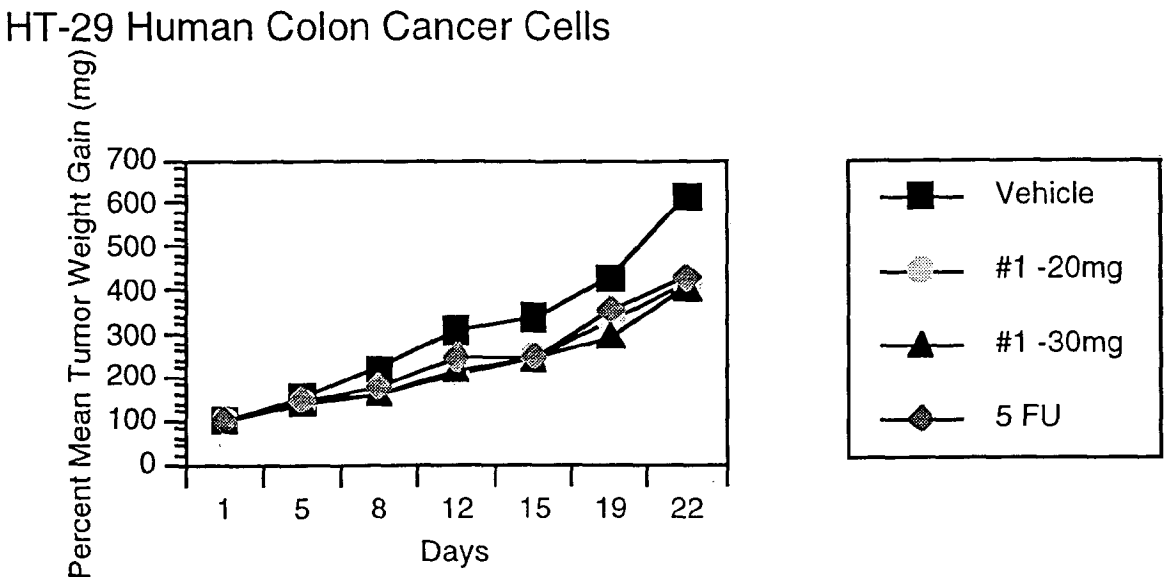


FIG. 9C